

AMENDMENTS TO THE CLAIMS

1.-25. (Canceled)

26. (Currently amended) A genetically modified mouse whose genome comprises a homozygous disruption of the endogenous Shp2 gene in at least a portion of neuronal forebrain cells such that no Shp2 is expressed in said portion of neuronal forebrain cells, wherein cells outside of the forebrain do not have a homozygous disruption of the endogenous Shp2 gene, and wherein said genetically modified mouse exhibits an increased body weight in comparison to a mouse whose genome does not comprise said disrupted Shp2 gene in said portion of neuronal forebrain cells.

27. (Canceled)

28. (Previously presented) The genetically modified mouse of Claim 26, wherein said mouse has early-onset obesity.

29. (Previously presented) The genetically modified mouse of Claim 26, wherein said mouse has a resistance to leptin in comparison to a wild-type mouse.

30. (Previously presented) The genetically modified mouse of Claim 26, wherein the Shp2 protein level is decreased by 50-70% in a forebrain lysate of said mouse in comparison to a wild-type mouse.

31. (Previously presented) The genetically modified mouse of Claim 26, wherein triglyceride levels are increased in the serum of said mouse in comparison to a wild-type mouse.

32-43. (Canceled)

44. (Previously presented) The genetically modified mouse of Claim 26, wherein insulin levels are increased in the serum of said mouse in comparison to a wild-type mouse.

45. (Previously presented) The genetically modified mouse of Claim 26, wherein the homozygous disruption of the endogenous Shp2 gene comprises a deletion of exon 4.

46. (Currently amended) A genetically modified mouse ~~comprising exhibiting~~ an increased body weight in comparison to a wild-type mouse, wherein neurons in at least a portion of the forebrain of said genetically modified mouse ~~has have~~ been genetically altered to lack expression of the endogenous Shp2 gene such that no Shp2 is expressed in said portion of the forebrain neurons, wherein cells outside of the forebrain are not genetically altered to lack expression of the endogenous Shp2 gene, and wherein said genetically modified mouse exhibits

an increased body weight in comparison to a mouse that expresses the endogenous Shp2 gene in said neurons in at least a portion of the forebrain.

47. (Previously presented) The genetically modified mouse of Claim 46, wherein said mouse has early-onset obesity.

48. (Previously presented) The genetically modified mouse of Claim 46, wherein said mouse has a resistance to leptin in comparison to a wild-type mouse.

49. (Previously presented) The genetically modified mouse of Claim 46, wherein the Shp2 protein level is decreased by 50-70% in a forebrain lysate of said mouse in comparison to a wild-type mouse.

50. (Previously presented) The genetically modified mouse of Claim 46, wherein triglyceride levels are increased in the serum of said mouse in comparison to a wild-type mouse.

51. (Previously presented) The genetically modified mouse of Claim 46, wherein insulin levels are increased in the serum of said mouse in comparison to a wild-type mouse.

52. (Previously presented) The genetically modified mouse of Claim 46, wherein the genetic alteration comprises a deletion of exon 4 in said endogenous Shp2 gene.

53. (Currently amended) A genetically modified mouse ~~comprising exhibiting~~ an increased body weight in comparison to a wild-type mouse, wherein the genome of the calcium/calmodulin-dependent protein kinase II alpha (CamK2a)-expressing cells in the forebrain of the genetically modified mouse ~~have been genetically~~ ~~has been~~ altered to lack expression of the endogenous Shp2 gene such that no Shp2 is expressed in the CamK2a-expressing forebrain cells, and wherein the genetically modified mouse exhibits an increased body weight in comparison to a mouse that expresses the endogenous Shp2 gene in CamK2a-expressing forebrain cells.

54. (Previously presented) The genetically modified mouse of Claim 53, wherein the mouse has early-onset obesity.

55. (Previously presented) The genetically modified mouse of Claim 53, wherein the mouse has a resistance to leptin in comparison to a wild-type mouse.

56. (Previously presented) The genetically modified mouse of Claim 53, wherein triglyceride levels are increased in the serum of the mouse in comparison to a wild-type mouse.

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57. (Previously presented) The genetically modified mouse of Claim 53, wherein insulin levels are increased in the serum of the mouse in comparison to a wild-type mouse.

58. (Previously presented) The genetically modified mouse of Claim 53, wherein the genetic alteration comprises a Cre-loxP-mediated truncation of the Shp2 gene.

59. (Previously presented) The genetically modified mouse of Claim 53, wherein the genetic alteration comprises a deletion of exon 4 in the endogenous Shp2 gene.